

METHOD OF TREATING FUMARATE HYDRATASE-DEFICIENT KIDNEY CANCER

SUMMARY

NCI scientists identified a tyrosine kinase inhibitor vandetanib that is highly cytotoxic to kidney cancer cells both in vitro and in vivo.

REFERENCE NUMBER

E-104-2014

PRODUCT TYPE

- Therapeutics

KEYWORDS

- tyrosine kinase inhibitor
- vandetanib
- kidney

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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DESCRIPTION OF TECHNOLOGY

Patients having germline fumarate hydratase ("FH") gene mutation are predisposed to develop aggressive kidney cancer with few treatment options and poor therapeutic outcomes. NCI scientists identified a tyrosine kinase inhibitor vandetanib that is highly cytotoxic to kidney cancer cells both in vitro and in vivo. C-Abl activity is upregulated in FH-deficient kidney tumors and vandetanib efficacy is a direct consequence of c-Abl inhibition. It was also found that combining metformin enhanced the cytotoxic effect of vandetanib by inhibiting NRF2 transcriptional activity in a SIRT1-dependent manner. Thus dual inhibition of c-Abl and NRF2 activity with vandetanib and metformin is a novel therapeutic approach to target glycolytically dependent, oxidatively stressed tumors. *In vitro* and *in vivo* data are available.

POTENTIAL COMMERCIAL APPLICATIONS

- Therapies for treating FH-deficient kidney cancer and glycolytically dependent, oxidatively stressed

tumors.

COMPETITIVE ADVANTAGES

- Specificity of mode of action may reduce potential side-effects • Novel mode of action may increase market competition • No effective therapy is currently available for patients with advanced FH-deficient kidney cancer.

INVENTOR(S)

[William Marston Linehan](#) (NCI) et al.

DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

Soubrier C, et al. Targeting ABL1-Mediated Oxidative Stress Adaptation in Fumarate Hydratase-Deficient Cancer. Cancer Cell. 8 December 2014. [PMID: 25490448](#).

PATENT STATUS

- **U.S. Filed:** US Patent Application No. 62/003,319 filed 27 May 2014
- **U.S. Filed:** Application # 62/003,319 filed on 27 May 2015

RELATED TECHNOLOGIES

- [E-201-2012 - Plant-derived Compounds for the Treatment of Retroviral Diseases](#)
- [E-042-2012 - Diabetes, Obesity, and Other Insulin-Related Diseases](#)

THERAPEUTIC AREA

- Cancer/Neoplasm